

LETTERS

VACCINATION AND RISK OF ALLERGIC DISEASE

In "Vaccination and Allergic Disease: A Birth Cohort Study," McKeever et al. reported strong crude and adjusted associations of vaccinations with asthma and eczema.¹ After stratifying on frequency of general practitioner (GP) visits, however, and finding that the strong associations were mostly confined to the lowest-frequency stratum, they concluded that ascertainment bias explains the associations in the total population. On the basis of their data and other studies, including ours,² they write, "current vaccination practices do not have an adverse effect on the incidence of allergic disease." However, a conclusion equally consistent with the evidence is that vaccinations may have adverse effects in at least some children.

First, the authors' interpretation of their stratified results may be misleading. Stratifying on a predictor of ascertainment does not always reduce ascertainment (misclassification) bias,³ and misclassification of both outcomes would have to be severely differential by vaccination status in the lowest GP-visit stratum to be consistent with their interpretation. Furthermore, the association between GP visits and outcome events may also reflect the effect of the latter on the former, which

means stratifying on visit frequency would increase bias if GP consultation is also associated with vaccination status. If visit frequency is affected by the outcome events, as expected, and assuming no confounding or other bias, then the crude associations are the best effect estimates.⁴ Moreover, consulting frequency may reflect true modifiers of the vaccination effects, rather than being only markers of ascertainment. Because of the imprecise estimation of effects within strata, the results are also consistent with vaccination effects in children with more frequent GP visits.

Regarding our study,² McKeever et al. state, "in general [Hurwitz and Morgenstern] found no association between vaccination and allergic disease." In fact, we detected associations between vaccination and allergy symptoms (adjusted odds ratio [OR]=1.63; 95% confidence interval [CI]=1.05, 2.54) and history (OR=1.69; 95% CI=1.10, 2.59), and we could not rule out effects on physician-diagnosed asthma. In its review of immunizations and immune dysfunction, the Institute of Medicine correctly reported that our findings favor an effect of diphtheria and tetanus toxoids and pertussis (DTP) or tetanus vaccination on clinical history of allergic disorder and cited inadequate literature to accept or reject a causal relation between immunizations and asthma.⁵

Addressing the possible causal role of vaccinations in subsequent allergic disease is difficult. Ethical issues preclude long-term randomized placebo-controlled trials, and estimates from observational studies are fraught with potential biases and alternative explanations. The current evidence, however, suggests that vaccinations may or may not increase the risk of allergic diseases. To conclude otherwise is misleading. ■

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